

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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POLOGNE

PCT

WRITTEN OPINION  
(PCT Rule 66)

		Date of mailing (day/month/year)	26.02.2004
Applicant's or agent's file reference ./.		REPLY DUE	within 3 month(s) from the above date of mailing.
International application No. PCT/PL 02/00056	International filing date (day/month/year) 24.07.2002	Priority date (day/month/year) 01.07.2002	
International Patent Classification (IPC) or both national classification and IPC A61K31/404			
Applicant PLIVA KRAKOW, ZAKLADY FARMACEUTYCZNE S.A. et al.			

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
  - I  Basis of the opinion
  - II  Priority
  - III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV  Lack of unity of invention
  - V  Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI  Certain documents cited
  - VII  Certain defects in the international application
  - VIII  Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.
 

**When?** See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also:** For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed,** the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 01.11.2004

Name and mailing address of the International preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Zimmer, B Formalities officer (incl. extension of time limits) Moranco Alcaine, N Telephone No. +49 89 2399-7462	
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**I. Basis of the opinion**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

**Description, Pages**

1-4 as originally filed

**Claims, Numbers**

1-4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5.  This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

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Novelty (N)	Claims
Inventive step (IS)	Claims 1-4
Industrial applicability (IA)	Claims

**2. Citations and explanations****see separate sheet**

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**Re Item V****Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Reference is made to the following documents:**

D1: EP-A-0 519 820 (ADIR) 23 December 1992 (1992-12-23) cited in the application

D2: DAMIEN, GERARD ET AL: 'Galenic development and pharmacokinetic profile of indapamide sustained release 1.5 mg' CLINICAL PHARMACOKINETICS (1999), 37(SUPPL. 1), 13-19 , XP009004369

**2. Novelty**

Prior art document D1 discloses sustained release tablets comprising 1.4% (w/w) indapamide as active ingredient as well as lactose (62 %), hypromellose (31 %), polyvidone (3 %) and the lubricants magnesium stearate (1.1 %) and colloidal silica (0.2 %) (ex. 1). The sustained release tablets disclosed in D2, which are prepared by wet granulation using water, differ from the subject-matter of the present application in that the amount of indapamide is below 1.5 % (table 1).

As the tablets disclosed in D1 lack copovidone as excipient and are prepared by wet granulation with a water/ alcohol solution the subject-matter of the present application seems to be new and thus fulfil the requirements of Art. 33(2) PCT in view of the cited prior art.

**3. Inventive Step**

Although the subject-matter of claim 1 of the present application seems to be new in view of the cited prior art it does not seem to be inventive for the following reasons (Art. 33(3) PCT):

D1 differs from the subject-matter of the present application in the pyrrolidone polymer excipient. Thus, the objective technical problem of the present application

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seems to be the provision of an alternative sustained release tablet formulation of indapamide.

The selection of copovidone (vinylpyrrolidone vinylacetate copolymer) instead of povidone (vinylpyrrolidone polymer) in the compositions of the present application seems to be arbitrary and cannot "prima facie" be regarded as inventive (Art. 33(3) PCT) for a person skilled in the art, in particular, as copovidone is a well known excipient of tablet formulations.

Furthermore, no convincing evidence (eg comparison tests showing an effect not derivable from the closest prior art) has been presented in order to show that an inventive step is necessary to use the claimed subject-matter for the solution of the posed problem.

If an inventive step is to be based on the presence of an unexpected effect this has to be proven by technical evidence; for instance by comparing the composition of Ex. 1 of D1 with the present application.

Dependent claims 2-3 do not appear to contain any additional features which involve an inventive step when combined with the subject-matter of any claim to which they refer. Dependent claims are only allowable when related to a patentable independent claim (Rule 6.4 PCT).

Independent process claim 4 also seems to be obvious for a person skilled in the art in view of the cited prior art document D2 (p. 14, right col.).